

## Amendments to the Claims

This listing of claims replaces all prior versions and listings of claims in the application.

### Listing of Claims

1. (Currently Amended) An isolated nucleic acid molecule consisting essentially of a nucleic acid sequence selected from the group consisting of:
  - a) at least ~~ten~~ fifteen contiguous nucleotides of SEQ ID NO:6, wherein said sequence includes nucleotide 32, 159, 298, 340, or 462 of SEQ ID NO:6, with the proviso that the nucleotide at position 32 is guanine, the nucleotide at position 159 is thymine, the nucleotide at position 298 is guanine, the nucleotide at position 340 is thymine, or the nucleotide at position 462 is guanine;
  - b) at least ~~ten~~ fifteen contiguous nucleotides of SEQ ID NO:1, wherein said sequence includes nucleotide 1895, 2254, 2510, or 2651 of SEQ ID NO:1, with the proviso that the nucleotide at position 1895 is thymine, the nucleotide at position 2254 is cytosine, the nucleotide at position 2510 is adenine, or the nucleotide at position 2651 is adenine;
  - c) at least ~~ten~~ fifteen contiguous nucleotides of SEQ ID NO:1, wherein said sequence includes nucleotide 3692 or 3693 of SEQ ID NO:1, with the proviso that the nucleotide at position 3692 is thymine or the nucleotide at position 3693 is adenine;
  - d) at least ~~ten~~ fifteen contiguous nucleotides of SEQ ID NO:1, wherein said sequence includes nucleotide 1102, 1301, 1303, 1464, or 1509 of SEQ ID NO:1, with the proviso that the nucleotide at position 1102 is thymine, the nucleotide at position 1301 is cytosine, the nucleotide at position 1303 is adenine, the nucleotide at position 1464 is adenine, or the nucleotide at position 1509 is adenine; and
  - e) the complement of a), b), c), or d).
2. (Canceled)
3. (Currently Amended) The isolated nucleic acid molecule of claim 1, wherein said nucleotide sequence is at least ~~ten~~ fifteen contiguous nucleotides of SEQ ID NO:1, wherein said sequence includes nucleotide 3692 or 3693 of SEQ ID NO:1, with the

proviso that the nucleotide at position 3692 is thymine or the nucleotide at position 3693 is adenine.

4. (Currently Amended) The isolated nucleic acid molecule of claim 1, wherein said nucleotide sequence is at least ~~ten~~ fifteen contiguous nucleotides of SEQ ID NO:1, wherein said sequence includes nucleotide 1895, 2254, 2510, or 2651 of SEQ ID NO:1, with the proviso that the nucleotide at position 1895 is thymine, the nucleotide at position 2254 is cytosine, the nucleotide at position 2510 is adenine, or the nucleotide at position 2651 is adenine.
5. (Currently Amended) The isolated nucleic acid molecule of claim 1, wherein said nucleotide sequence is at least ~~ten~~ fifteen contiguous nucleotides of SEQ ID NO:1, wherein said sequence includes nucleotide 1102, 1301, 1303, 1464, or 1509 of SEQ ID NO:1, with the proviso that the nucleotide at position 1102 is thymine, the nucleotide at position 1301 is cytosine, the nucleotide at position 1303 is adenine, the nucleotide at position 1464 is adenine, or the nucleotide at position 1509 is adenine.
6. (Currently Amended) The isolated nucleic acid molecule of claim 1, wherein said nucleotide sequence is at least ~~ten~~ fifteen contiguous nucleotides of SEQ ID NO:6, wherein said sequence includes nucleotide 32 of SEQ ID NO:6, with the proviso that the nucleotide at position 32 of SEQ ID NO:6 is guanine.
7. (Currently Amended) The isolated nucleic acid molecule of claim 1, wherein said nucleotide sequence is at least ~~ten~~ fifteen contiguous nucleotides of SEQ ID NO:6, wherein said sequence includes nucleotide 159 of SEQ ID NO:6, with the proviso that the nucleotide at position 159 of SEQ ID NO:6 is thymine.
8. (Currently Amended) The isolated nucleic acid molecule of claim 1, wherein said nucleotide sequence is at least ~~ten~~ fifteen contiguous nucleotides of SEQ ID NO:6, wherein said sequence includes nucleotide 298 of SEQ ID NO:6, with the proviso that the nucleotide at position 298 of SEQ ID NO:6 is guanine.

9. (Currently Amended) The isolated nucleic acid molecule of claim 1, wherein said nucleotide sequence is at least ~~ten~~ fifteen contiguous nucleotides of SEQ ID NO:6, wherein said sequence includes nucleotide 340 of SEQ ID NO:6, with the proviso that the nucleotide at position 340 of SEQ ID NO:6 is thymine.
10. (Currently Amended) The isolated nucleic acid molecule of claim 1, wherein said nucleotide sequence is at least ~~ten~~ fifteen contiguous nucleotides of SEQ ID NO:6, wherein said sequence includes nucleotide 462 of SEQ ID NO:6, with the proviso that the nucleotide at position 462 of SEQ ID NO:6 is guanine.
11. (Original) An isolated nucleic acid encoding a PNMT polypeptide, wherein said polypeptide comprises a PNMT amino acid sequence variant relative to the amino acid sequence of SEQ ID NO:8, and wherein said amino acid sequence variant is at a residue selected from the group consisting of 9, 98, and 112.
12. (Original) The isolated nucleic acid of claim 11, wherein said amino acid sequence variant is a serine at residue 9, an alanine at residue 98, or a cysteine at residue 112.
13. (Withdrawn) An isolated PNMT polypeptide, wherein said polypeptide comprises a PNMT amino acid sequence variant relative to the amino acid sequence of SEQ ID NO:8, wherein said amino acid sequence variant is at a residue selected from the group consisting of 9, 98, and 112.
14. (Withdrawn) The isolated polypeptide of claim 13, wherein said amino acid sequence variant is a serine at residue 9, an alanine at residue 98, or a cysteine at residue 112.
15. (Withdrawn) The isolated polypeptide of claim 13, wherein activity of said polypeptide is altered relative to a wild type PNMT polypeptide.
16. (Canceled)
17. (Withdrawn) A method for determining if a subject is predisposed to a disease, wherein said method comprises:

- a) obtaining a biological sample from said mammal, and
  - b) detecting the presence or absence of a *PNMT* nucleotide sequence variant in said sample, wherein predisposition to said disease is determined based on the presence or absence of said variant.
- 18. (Withdrawn) The method of claim 17, wherein said method further comprises detecting the presence or absence of a plurality of said *PNMT* nucleotide sequence variants in said sample to obtain a variant profile of said subject, and wherein predisposition to said disease is determined based on said variant profile.
- 19. (Withdrawn) The method of claim 18, wherein said disease is a multiple sclerosis.
- 20. (Withdrawn) The method of claim 18, wherein said disease is early onset Alzheimer's disease.
- 21. (Withdrawn) A method for assisting a medical or research professional, wherein said method comprises:
  - a) obtaining a biological sample from a subject, and
  - b) detecting the presence or absence of a plurality of *PNMT* nucleotide sequence variants in said sample to obtain a variant profile of said subject.
- 22. (Withdrawn) The method of claim 21, wherein said method further comprises communicating said profile to said medical or research professional.
- 23. (Withdrawn) A method for determining the methyltransferase status of an individual, said method comprising determining whether said subject comprises a variant *PNMT* nucleic acid.
- 24. (Withdrawn) A method for predicting the therapeutic efficacy of a compound in a subject, wherein metabolism of said compound comprises methylation, said method comprising:
  - a) determining the methyltransferase status of said subject; and

- b) correlating said methyltransferase status with the ability of said subject to metabolize said compound, wherein said compound is predicted to be therapeutically effective if said methyltransferase status is enhanced in said subject, and wherein said compound is predicted not to be therapeutically effective if said methyltransferase status is reduced in said subject.
25. (Withdrawn) The method of claim 24, wherein said determining of said methyltransferase status comprises determining whether said subject comprises a variant *PNMT* nucleic acid.
26. (Withdrawn) The method of claim 25, wherein said variant *PNMT* nucleic acid comprises a non-synonymous single nucleotide polymorphism.
27. (Withdrawn) The method of claim 24, wherein said determining of said methyltransferase status comprises measuring methyltransferase activity in a biological sample from said subject.
28. (Withdrawn) The method of claim 27, wherein said methyltransferase activity is *PNMT* activity.
29. (Withdrawn) A method for predicting the therapeutic efficacy of a compound in a subject, wherein metabolism of said compound comprises methylation, said method comprising:
- a) estimating the level of methyltransferase activity in said subject; and
  - b) correlating said level of methyltransferase activity with the ability of said subject to metabolize said compound, wherein said compound is predicted to be therapeutically effective if said level of methyltransferase activity is increased in said subject, and wherein said compound is predicted not to be therapeutically effective if said level of methyltransferase activity is reduced in said subject.
30. (Withdrawn) The method of claim 29, wherein said methyltransferase is *PNMT*.

31. (Withdrawn) The method of claim 30, wherein said methyltransferase activity is estimated in vitro in a biological sample from said subject.
32. (Withdrawn) The method of claim 29, wherein said level of methyltransferase activity in said subject is estimated by determining whether said subject comprises a variant *PNMT* nucleic acid.
33. (Withdrawn) The method of claim 32, wherein said variant *PNMT* nucleic acid comprises a non-synonymous single nucleotide polymorphism.
- 34-37. (Canceled)
38. (Currently Amended) The isolated nucleic acid molecule of claim 1, wherein said isolated nucleic acid molecule is from ~~40~~ 15 to 100 nucleotides in length.
39. (Previously Presented) The isolated nucleic acid molecule of claim 1, wherein said isolated nucleic acid molecule is from 20 to 50 nucleotides in length.
40. (Previously Presented) A vector comprising the nucleic acid molecule of claim 1.
41. (Previously Presented) The vector of claim 40, wherein said nucleic acid molecule is from 20 to 50 nucleotides in length.